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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/077,214	05/26/1998	WALTER SCHMIDT	0652.1710000	5745

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EXAMINER	
SCHWADRON, RONALD B	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 10/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/077,214	SCHMIDT ET AL.	
	Examin r	Art Unit	
	Ron Schwadron, Ph.D.	1644	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence ddress --

THE REPLY FILED 14 July 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☒ A Notice of Appeal was filed on *7/14/2003*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☐ The proposed amendment(s) will not be entered because:

   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____.

3. ☒ Applicant's reply has overcome the following rejection(s): see enclosed action.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *see enclosed action*.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: _____.

   Claim(s) rejected: *36,38-40,42-44,48-50,69 and 70*.

   Claim(s) withdrawn from consideration: *37,41,45-47,51-68*.

8. ☐ The proposed drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☐ Other: _____

RONALD B. SCHWADRON
PRIMARY EXAMINER
GROUP ~~1800~~ 1600

1. Claims 36,38-40,42-44,48-50,69,70 are under consideration. Claims 69 and 70 have been amended.

2. The rejection of claims 69 and 70 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the reasons elaborated in the previous Office Action is withdrawn in view of the amendment to claim 69 as per the instant amendment.

3. The rejection of claims 69 and 70 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the reasons elaborated in the previous Office Action is withdrawn in view of the amendment to claim 69 as per the instant amendment.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was

made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 36,38-40,42-44,48-50,69,70 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Nair et al. in view of Fearon et al., Townsend et al., Van Der Bruggen et al. and prior art disclosed in the specification (see page 3) for the reasons elaborated in the previous Office Action.

Nair et al. disclose use of an organic polycation (eg. cationic liposomes) to deliver an MHC class I antigen to tumor cells (see abstract). The organic polycation used by Nair et al. contains polylysine conjugated to another molecule (see abstract and page 238, second column, last paragraph). Nair et al. teach that said method is an efficient means of sensitizing target cells for CTL lysis in the context of MHC class I (see page 242, last sentence). Nair et al. do not disclose human tumor cells treated to express influenza virus peptide in the context of HLA class I. Fearon et al. teach a tumor vaccine wherein tumor cells are transfected with the gene encoding HA (see entire paper). HA is a viral antigen. Townsend et al. teach that influenza HA or NP peptides are recognized by CTL in the context of MHC class I. Van Der Bruggen et al. teach MHC class I restricted tumor antigens and that such antigens can be used to provoke CTL in vivo (see page 15, second paragraph). Van Der Bruggen et al. teach that said peptides can be delivered by vector (to infect APC) or by direct administration of the peptide to APC (see page 15, second paragraph). The art recognizes that tumors express numerous different tumor associated antigens (see prior art disclosed in specification, page 3). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Nair et al. disclose use of an organic polycation (eg. cationic liposomes containing polylysine) to deliver an MHC class I antigen to tumor cells, Fearon et al. teach a tumor vaccine wherein tumor cells are transfected with the gene encoding HA while Van Der Bruggen et al. teach MHC class I restricted tumor antigens and that such antigens can be used to provoke CTL

in vivo. In view of the fact that the cells disclosed by Nair et al. were treated with intact protein, said cells would have been expected to present multiple different peptides representing different epitopes derived from said molecule. It would also be expected that HA would encode a variety of different epitopes that would bind different HLA molecules found on MHC antigen heterozygous human tumor cells. One of ordinary skill in the art would have been motivated to do the aforementioned because of the demonstration by Fearon et al. of the use of HA transfected tumor cells as a tumor vaccine, while Nair et al. teach that their method is an efficient means of sensitizing target cells for CTL lysis in the context of MHC class I. Regarding the "allogeneic" tumor vaccine limitation, the recitation of an intended use (eg. delivery to an allogenic host) carries no patentable weight in this product claim. Regarding the limitation of claim 70, the recitation of a method wherein the claimed product is made carries no patentable weight in the instant product claims because the claimed product appears to be the same irregardless of how it is made (eg. loaded with peptide via incubation with polylysine versus loaded with peptide via incubation with transferrin/polylysine).

Regarding applicants comments about Nair et al. and MHC binding by the peptide, the recitation of a method wherein the instant product is made carries no patentable weight in the instant product claims because the prior art product rendered obvious in the instant rejection is the same as the claimed invention. While Nair et al. initially add full length protein, *Nair et al. discloses that said protein is internalized into the cell and processed to yield peptides which bind MHC class I (eg. see Nair et al., abstract and column two, page 241, Discussion section, continued on next page)*. Regarding motivation to create the claimed invention, one of ordinary skill in the art would have been motivated to do the aforementioned because of the demonstration by Fearon et al. of the use of HA transfected tumor cells as a tumor vaccine, while Nair et al. teach that their method is an efficient means of sensitizing target cells for CTL lysis in the context of MHC class I. Nair et al. and Fearon et al. both teach that the immunogenicity of tumor cells can be increased by adding additional exogenous antigens to said tumor cells. One of ordinary skill in the art at the time the invention was made would have a reasonable expectation of success of producing the claimed invention because *Fearon et al. teach use of HA transfected tumor cells as a tumor vaccine, while Nair et al. teach that their method is an efficient means of sensitizing target cells for CTL lysis in the context of MHC class I.* While Nair et al. do not disclose human tumor cells treated to express influenza virus peptide in the context of HLA class I, Fearon et al. teach a tumor vaccine wherein tumor cells

are transfected with the gene encoding HA (see entire paper). HA is a viral antigen. Townsend et al. teach that influenza HA or NP peptides are recognized by CTL in the context of MHC class I. Van Der Bruggen et al. teach MHC class I restricted tumor antigens and that such antigens can be used to provoke CTL in vivo (see page 15, second paragraph). Van Der Bruggen et al. teach that said peptides can be delivered by vector (to infect APC) or by direct administration of the peptide to APC (see page 15, second paragraph). The art recognizes that tumors express numerous different tumor associated antigens (see prior art disclosed in specification, page 3). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Nair et al. disclose use of an organic polycation (eg. cationic liposomes containing polylysine) to deliver an MHC class I antigen to tumor cells, Fearon et al. teach a tumor vaccine wherein tumor cells are transfected with the gene encoding HA while Van Der Bruggen et al. teach MHC class I restricted tumor antigens and that such antigens can be used to provoke CTL in vivo.

6. No claim is allowed.

7. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Dr. Ron Schwadron whose telephone number is (703) 308-4680. The examiner can normally be reached Monday through Thursday from 7:30 to 6:00. A message may be left on the examiners voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Ms Christina Chan can be reached on (703) 308-3974. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703) 308-0196.

Ron Schwadron, Ph.D.
Primary Examiner
Art Unit 1644

RONALD SCHWADRON
PRIMARY EXAMINER
GROUP 1600 1600